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January 30, 2004

Dockets Management Branch, HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. 02P-0406
Comment to Suitability Petition

Dear Sir or Madam:

We are writing on behalf of GlaxoSmithKline (GSK) regarding the comment submitted by The Weinberg Group on November 19, 2003, to the above-referenced suitability petition (the Comment). This petition, submitted by The Weinberg Group on September 10, 2002, sought a declaration that amoxicillin/clavulanate potassium tablets for oral suspension 200 mg/28.5 mg, 400 mg/57 mg, and 600 mg/42.9 mg are suitable for submission in abbreviated new drug applications (ANDAs) (the Petition).

According to the Comment, the Food and Drug Administration (FDA) informed The Weinberg Group, by telephone, that the proposed 200 mg/28.5 mg and 400 mg/57 mg tablets for oral suspension may be suitable for ANDA submission only if the reference drug is changed to Augmentin® chewable tablets. Our understanding, based on the description of the telephone call in the Comment, is that FDA has effectively denied the Petition.

For the reasons stated below, GSK supports FDA's apparent decision to deny the Petition, insofar as The Weinberg Group sought permission to submit ANDAs referencing Augmentin® and Augmentin ES-600™ powder for oral suspension. We respectfully request, however, that the agency articulate the reasons for its denial in a written submission to the docket. Thereafter, The Weinberg Group may seek formal reconsideration of FDA's decision, or submit a

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new suitability petition requesting permission to reference Augmentin® chewable tablets.

I. The Weinberg Group Must Seek Formal Reconsideration of FDA's Decision or Submit a New Suitability Petition

The Weinberg Group's original suitability petition requested that FDA "declare that the drug product Amoxicillin and Clavulanate Potassium Tablets for Oral Suspension 200 mg/28.5 mg, 400 mg/57 mg and 600 mg/42.9 mg are suitable for submission as an abbreviated new drug application (ANDA)." Petition at 1; *see* 21 USC 355(j)(2)(C) (2002). The reference drugs cited in the Petition were GSK's Augmentin® powder for oral suspension 200 mg/28.5 mg and 400 mg/57 mg and Augmentin ES-600™ powder for oral suspension 600 mg/42.9 mg. *See* Petition at 1.

On November 19, 2003, The Weinberg Group submitted a comment to the docket, which states that:

> In a recent telephone communication, FDA indicated that the 200 mg/28.5 mg and 400 mg/57 mg strengths of the proposed product may be declared suitable for submission as an ANDA if the Reference Listed Drug (RLD) were changed from Augmentin Suspension to Augmentin Chewable tablets. The purpose of this letter is to examine further the appropriate RLD for the 200 mg/28.5 mg and 400 mg/57 mg products.

Comment at 1.

Based on The Weinberg Group's own discussion, it appears that FDA has constructively denied the Petition, which sought permission to submit ANDAs referencing Augmentin® and Augmentin ES-600™ powder for oral suspension. Moreover, The Weinberg Group appears to have abandoned the proposed 600 mg/42.9 mg tablets for oral suspension, because the Comment omits all discussion of the product, and characterizes the reference drug only as "Augmentin® Suspension 200 mg/28.5 mg per 5ml and 400 mg/57 mg per 5ml." *Id.* To date, no written denial has been placed in the docket. *See* 21 CFR 10.30(e)(3) (requiring a written response to each petition).

The Weinberg Group's comment continues by "request[ing] that the Agency reconsider this position" and setting forth the grounds for such

reconsideration. Comment at 2. The Weinberg Group is not permitted to seek reconsideration of FDA's denial in this manner, however.

Under the agency's regulations, a person may request reconsideration of part or all of FDA's decision on a petition, but must do so in a separate petition for reconsideration. *See* 21 CFR 10.33(b). If that request relies on information not present in the administrative record, it must be filed as a new petition to modify the decision. *See id.* at 10.33(e). The Weinberg Group may, of course, seek to submit an ANDA referencing Augmentin® chewable tablets, but must do so through a new suitability petition. *See id.* at 314.93 (requiring a suitability petition to identify the precise listed drug to which a change is being proposed). In either case, the Comment submitted by The Weinberg Group is contrary to FDA's procedural rules.

II. The Comment Confirms Why the Proposed Product Cannot Reference Augmentin® Powder for Oral Suspension

Putting aside the procedural concerns, the Comment continues to demonstrate why the proposed product cannot reference Augmentin® powder for oral suspension.

First, The Weinberg Group argues that the tablets for oral suspension are not intended to be therapeutically equivalent to Augmentin®, but rather to offer an alternative "therapeutic modality." Comment at 1. This statement echoes The Weinberg Group's previous argument that the product is designed to provide an alternate dosage form and "is targeted only for that population of patients in which a full-tablet, or multiples thereof, are recommended." Comment to Docket No. 02P-0406 (May 16, 2003) at 4. These comments once again concede that the proposed product cannot be dosed according to the Augmentin® powder for oral suspension dosing regimen.

The Weinberg Group's solution is to label the product for use only in those patients whose weights match the "full-tablet increments" offered by the tablets for oral suspension. *See id.* at 4-5. This is simply implausible and unsafe for a drug intended for use in children as young as three months. For example, Augmentin® powder for oral suspension is dosed for most infections at 45 mg/kg/day, divided every 12 hours. *See* Augmentin® Labeling, *Dosage and Administration* (2003) (attached). Under this dosing schedule, the tablets for oral suspension could only be approved for children weighing 9, 18, 27, and 36 kg (200, 400, 600, and 800 mg tablets (by amoxicillin) at 45 mg/kg/day, divided every 12 hours). To our

knowledge, FDA has never approved a generic drug for use in such a small and discontinuous subset of a reference drug's target population.

Alternatively, to the extent that The Weinberg Group intends the product to be dosed according to a "flatter" schedule than that approved for Augmentin®, it is impermissible as a matter of law. *See* 21 CFR 314.93(a) ("Petitions to submit abbreviated new drug applications for other changes from a listed drug will not be approved."); *see also* Letters from G. Buehler, Docket Nos. 01P-0130 & 01P-0283 (July 9 & 3, 2002) (denying petitions and stating that "a change in dosing regimen is not petitionable under Section 505(j)(2)(C) of the Act.").

Finally, The Weinberg Group asserts that the proposed product offers a number of features "unique" from Augmentin® powder for oral suspension, which "result in benefits to the consumer that are not available with a conventional suspension dosage." Comment at 2. The Weinberg Group claims that the proposed product offers "[b]etter precision of dosage[.]" *Id.* As described above and in our previous submission to the docket, the proposed product's unit dosing is in no way more precise than that of Augmentin® powder for oral suspension. Rather, it prevents the product from being dispensed according to the approved dosing regimen. And, The Weinberg Group claims that the proposed product offers the advantage of "[e]asy administration to patients who have difficulty swallowing." *Id.* This, too, is incorrect. Both Augmentin® powder for oral suspension and the tablets for oral suspension are ultimately consumed by the patient as a liquid.

III. Conclusion

For the reasons discussed above, we respectfully request that the agency issue a written decision denying the Petition. Until such a written decision issues, it is inappropriate for The Weinberg Group to seek reconsideration or otherwise continue to press its arguments before FDA.

Sincerely,

DM Fox /BMC

David M. Fox

Attachment

cc: Gary Buehler, Director, Office of Generic Drugs, HFD-600
Martin Shimer, Senior Regulatory Manager, HFD-615
Emily Thomas, Regulatory Officer, HFD-615